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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,838	02/22/2000	PAULUS HUBERTUS, ANDREAS QUAX	2212.135/00	7213

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,838	QUAX ET AL.	
	Examiner	Art Unit	
	Robert M Kelly	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Due to the missing papers in the file, and in order to set the record straight, the prior restriction requirements are withdrawn.

Applicant's attorney of record, Mr. Londa, was contacted on 7 October 2004 and it was agreed that the attorney would send a copy of the claims and preliminary amendments so that the claims which are of record could be verified with the claims listed in the Application file. The claims appear to be in agreement.

The following lists the claims as is understood to be the currently amended version by the Examiner:

1. A recombinant nucleic acid molecule comprising a vector useful for transfection or transduction of mammalian, e.g. human, cells, wherein said vector contains a nucleic acid insertion encoding an expressible hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function.

2. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with a binding function comprises a receptor binding domain.

3. A recombinant nucleic acid molecule according to Claim 2, wherein said receptor binding domain is selected from the group consisting of urokinase receptor binding domain of urokinase, receptor binding domain of epidermal growth factor, receptor associated protein that binds to LDL Receptor related protein (α_2-macroglobulin receptor) and VLDL Receptor.

4. A recombinant nucleic acid molecule according to Claim 2, wherein said receptor binding domain comprises the aminoterminal part of urokinase which is capable of binding to the urokinase receptor.

5. A recombinant nucleic acid molecule according to Claim 2, wherein said receptor binding domain comprises amino acid residues 1 through 135 of urokinase.

6. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with an effector function is an enzymatically active domain.

7. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with an effector function has protease inhibitor activity.

8. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises a protease inhibitor or active part thereof, said protease inhibitor being selected from the group consisting of (bovine) pancreatic trypsin inhibitor, (bovine) splenic trypsin inhibitor, urinary trypsin inhibitor, tissue inhibitor of matrix metalloproteinase 1, tissue inhibitor of matrix metalloproteinase 2, tissue inhibitor of matrix metalloproteinase 3, and elastase inhibitor.

9. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises (amino acid residues 53 through 94 of) mature bovine pancreatic trypsin inhibitor.

10. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises bovine splenic trypsin inhibitor.

11. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises a tissue inhibitor of matrix metalloproteinases.

12. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with an effector function comprises (an active part of) two or more different protease inhibitors, or two or more copies of (an active part of) a protease inhibitor, or both.

13. A recombinant nucleic acid molecule according to Claim 1, wherein said vector is selected from the group consisting of viral and non-viral vectors useful for transfection or transduction of mammalian cells.

14. A recombinant nucleic acid molecule according to Claim 1, wherein said vector is an adenovirus vector or a retrovirus vector useful for the transfection or transduction of human cells.

15. A recombinant nucleic acid molecule according to Claim 1, wherein said vector is an adenovirus vector based on shuttle vector pMAD5.

16. A recombinant nucleic acid molecule according to Claim 1, wherein said nucleic acid insertion encoding an expressible hybrid polypeptide or protein is under the control of a cell- or tissue-specific promoter.

17. A recombinant nucleic acid molecule according to Claim 1, wherein said nucleic acid insertion encoding an expressible hybrid polypeptide or protein is under the control of an endothelial cell-specific promoter, or a vascular smooth muscle cell-specific promoter, or a liver-specific promoter.

18. A recombinant nucleic acid molecule comprising a vector useful for transfection or transduction of mammalian, e.g. human, cells, wherein said vector contains a nucleic acid insertion encoding an expressible hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, wherein the domain with a binding function is a cell surface receptor binding domain.

19. A recombinant nucleic acid molecule comprising a vector useful for transfection or transduction of mammalian, e.g. human, cells, wherein said vector contains a nucleic acid

insertion encoding an expressible hybrid polypeptide or protein which comprises a receptor binding domain selected from the group consisting of urokinase receptor binding domain of urokinase, receptor binding domain of epidermal growth factor, receptor associated protein that binds to LDL Receptor related protein ((α_2-macroglobulin receptor) and VLDL Receptor, and a domain with protease inhibitor activity which comprises a protease inhibitor or active part thereof, said protease inhibitor being selected from the group consisting of (bovine) pancreatic trypsin inhibitor, (bovine) splenic trypsin inhibitor, urinary trypsin inhibitor, tissue inhibitor of matrix metalloproteinase 1, tissue inhibitor of matrix metalloproteinase 2, tissue inhibitor of matrix metalloproteinase 3, and elastase inhibitor.

20. A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in Claim 1 to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

21. A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or transducing mammalian cells with a recombinant nucleic acid molecule as claimed in Claim 1 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

22. A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in

Claim 18 to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

23. A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in Claim 19 to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

24. A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or transducing mammalian cells with a recombinant nucleic acid molecule as claimed in Claim 18 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

25. A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or transducing mammalian cells with a recombinant nucleic acid molecule as claimed in Claim 19 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

In view of the claims, as listed above, the following elections are required.

Election/Restrictions

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Claims 3 and 19 are drawn to four different domains with a binding function; and

Claims 8 and 19 are drawn to seven different domains with a protease inhibiting function.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claim(s) are generic: 1, 2, and 7.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the special technical feature shared between any two or more groups is a nucleic acid encoding a fusion protein comprising a domain with a binding function and a domain with a protease inhibiting function. WIPO Document No. WO 92/02553 to Ballance, et al., published 20 February 1992 (provided in Applicant's IDS, and therefore is not listed in a notice of references cited but with be addressed in the Official Action on the merits) provides for proteins and nucleic acids encoding a region which binds a tumor and a region which inhibits a protease (ABSTRACT). Hence, the special technical feature is taught by Ballance. Moreover, each of the listed inhibitors and binding regions bind different receptors,

and hence, has a special technical feature not taught by the other groups. Therefore, the species do not relate to a single general inventive concept.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M Kelly whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER